



**1993 Falk Memorial Lecture.** (left to right) Lecture coordinator Elizabeth Murphy; lecturer Roger Y. Tsien; Director Kenneth Olden; Falk's widow, Gabrielle Falk; Falk's son, Donald H. Falk; and Falk's sister, Eva Wulkan.

account for only 15% of all colorectal cancers, it is likely that both inheritance and environmental factors play important roles in the pathogenesis of this disease.

Scientists at NIEHS organized an interactive workshop last fall among researchers in environmental carcinogenesis and those studying the molecular biology of colorectal cancer to examine potential interactions between environmental factors and molecular genetics in this cancer.

At the workshop, June Dunnick, one of the workshop organizers, with Dale Sandler and Ronald Melnick and NIEHS colleague Michael R. Elwell, reviewed studies done within the Department of Health and Human Services primarily at NIEHS as a part of the National Toxicology Program. Of 435 chemicals tested in long-term rodent studies by National Cancer Institute, and later by NTP, 14 have shown some evidence for colorectal cancer in the rat. Colorectal cancer is rarely found as a spontaneous tumor in these rodent models, occurring in the historical database at an incidence of less than 0.1%. Future research will include studies to characterize the spectrum of genetic changes in colorectal cancers induced by bromodichloromethane and other brominated chemicals.

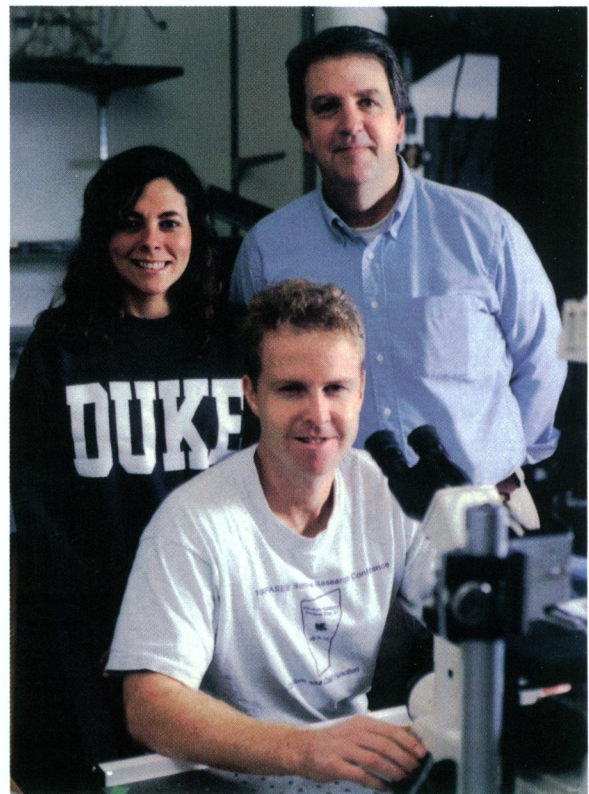
Dunnick noted, "Further research on the metabolism of brominated chemicals is needed to identify specific enzyme systems involved." She said that studies are being conducted by Robert Langenbach at NIEHS using isolated cell cultures with specific P450 isozymes to identify P450-dependent mutational changes caused by brominated chemicals that may reflect early genetic events in the multistep carcinogenic process.

Epidemiologists at the workshop recommended that epidemiology studies be

expanded to geographic areas where there are high exposures to trihalomethanes and to other sources of exposure to brominated chemicals. Melnick stated that interrelating the findings from toxicology, epidemiology, and molecular biology studies will help elucidate the contribution of environmental factors in colorectal cancer.

**Tsien Delivers Falk Lecture**  
Roger Y. Tsien, currently professor in the Departments of Pharmacology and Chemistry at the University of California, San Diego, and an investigator of the Howard Hughes Medical Institute, gave the ninth Hans L. Falk Memorial Lecture 17 November 1993 at NIEHS. Hans L. Falk, the internationally known environmental health science authority for whom the lecture is named, was one of the first scientific staff members of NIEHS and one of its founding members and shaping forces.

In his lecture, "How Cells Compartmentalize Internal Messengers: An Imaging Perspective," Tsien discussed his work on the design, synthesis, and application of fluorescent indicators for monitoring intracellular ions and messengers such as calcium, sodium, and cyclic AMP. Using video and slides, Tsien illustrated many examples of how these fluorescent indicators can be used in understanding cell communication. He illustrated the role of calcium in the immune response by showing that a rise in calcium, viewed in real time with the fluorescent indicator fura-2, occurs in T-lymphocytes as they kill their target cells.



**Cell scientists.** Carla M.P. Ribeiro and Gary S.J. Bird (standing) work with James W. Putney, chief of the Laboratory of Cellular and Molecular Pharmacology.

mammalian cells will greatly expand the use of fluorescent indicators.

## How Cells Regulate Calcium

Scientists have for some time appreciated the importance of calcium in cell biology, especially in the cellular actions of toxic substances. In the 9 December 1993 issue of *Science*, James Putney of NIEHS reviewed the work from his group as well as two recent reports published in *Nature* by C. Randriamampita and R. Y. Tsien and A.B. Parenkh et al. that detail breakthroughs which may lead to a better understanding of these processes.

In normal, healthy cells, the concentration of calcium in the cytoplasm is regulated within rather narrow limits and at a very low level, about 1/10,000 of the concentration in the blood. Hormones and growth factors may transiently increase this level of calcium as part of a signaling mechanism, which is important in a large variety of cellular response patterns including the signal for cells to grow or differentiate appropriately.

However, aberrant, inappropriate increases in calcium in the cytoplasm of cells can lead to cell death or to misdirected growth and oncogenesis. When hormones, growth factors, and other chemicals regulate cell calcium, they do so by regulating the release of calcium from intracellular organelles and also by regulat-